

PTO/SB/08A (10-01)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Please type a plus sign (+) inside this box



PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 5

Complete if Known

Application Number 09/780,675
Filing Date February 12, 2001
First Named Inventor NICOLAIDES et al.
Group Art Unit 164T 1636
Examiner Name Unassigned
Attorney Docket Number 01107.00098

RECEIVED
AUG 20 2001
TECH CENTER 1600/2900

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			
TMT		5,907,079		Mak et al.	05/25/1999	—
TMT		6,146,894		Nicolaides et al.	11/14/2000	—
TMT		6,191,268	B1	Liskay et al.	02/20/2001	—

FOREIGN PATENT DOCUMENTS

Examiner Initials *	Cite No. ¹	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ₆
		Office ³	Number ⁴	Kind Code ⁵ (if known)				
TMT		PCT	WO 99/19492		Betzner et al. Doutriaux	04/22/1999	—	
TMT		PCT	WO 97/08312		Kinzel et al. Vogelstein	03/06/1997	—	

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
TMT		Allen, D., et al., "MutS mediates heteroduplex loop formation by a translocation mechanism" <i>EMBO J.</i> , 1997, 16(14), 4467-4476.	
TMT		Baker, S.M., et al., "Male mice defective in the DNA mismatch repair gene PMS2 exhibit abnormal chromosome synapsis in meiosis" <i>Cell</i> , 1995, 82, 309-319.	
TMT		Bronner C.E., et al., "Mutation in the DNA mismatch repair gene homologue hMLH1 is associated with hereditary non-polyposis colon cancer" <i>Nature</i> , 1994, 368, 258-261.	
TMT		de Wind, N., et al., "Inactivation of the mouse Msh2 gene results in mismatch repair deficiency, methylation tolerance, hyperrecombination, and predisposition to cancer" <i>Cell</i> , 1995, 82, 321-330.	
TMT		Drummond, J.T., et al., "Isolation of an hMSH2-p160 heterodimer that restores DNA mismatch repair to tumor cells" <i>Science</i> , 1995, 268, 1909-1912.	
TMT		Drummond, J.T., et al., "Cisplatin and adriamycin resistance are associated with mutla and mismatch repair deficiency in an ovarian tumor cell line" <i>J. Biological Chemistry</i> , 1996, 271(33), 19645-19648.	
TMT		Edelmann, W., et al., "Meiotic pachytene arrest in MLH1-deficient mice" <i>Cell</i> , 1996, 85, 1125-1134.	
TMT		Eshleman, J.R., et al., "Mismatch repair defects in human carcinogenesis" <i>Human Molecular Genetics</i> , 1996, 5, 1489-1494.	
duplicate		Fishel, R. et al. "The human mutator gene homolog MSH2 and its association with hereditary nonpolyposis colon cancer." <i>Cell</i> 1993, 7:1027-1038.	

Examiner
Signature

[Signature]

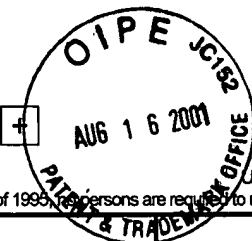
Date
Considered

July 12, 2002

412883-1

Part of Paper 8

Please type a plus sign (+) inside this box →



PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 2 of 5

Complete if Known

Application Number	09/780,675
Filing Date	February 12, 2001
First Named Inventor	NICOLAIDES et al.
Group Art Unit	184T 1636
Examiner Name	Unassigned
Attorney Docket Number	01107.00098

RECEIVED
AUG 20 2001
TECH CENTER
1600/2900

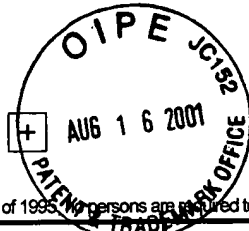
OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
mmf		Galio, L., et al., "ATP hydrolysis-dependent formation of a dynamic ternary nucleoprotein complex with MutS and MutL" <i>Nucleic Acids Research</i> , 1999 , 27(11), 2325-2331.	
mmf		Hamilton, S.R. et al. "The molecular basis of Turcot's syndrome." <i>N. Eng. J. Med.</i> 1995 , 332:839-847.	
mmf		Harfe, B.D. et al. "DNA mismatch repair and genetic instability" <i>Annu. Rev. Genet.</i> , 2000 , 34, 359-399.	
mmf		Hoang J., et al., "BAT-26, an Indicator of the Replication Error Phenotype in Colorectal Cancers and Cell Lines" <i>Cancer Res.</i> , 1997 , 57, 300-303.	
mmf		Holmes, J., S. Clark, and P. Modrich. "Strand-specific mismatch correction in nuclear extracts of human and <i>Drosophila melanogaster</i> cell lines" <i>Proc. Natl. Acad. Sci. USA</i> 1990 87:5837-5841.	
mmf		Honma, M. et al., "Cytotoxic and Mutagenic Responses to X-rays and Chemical Mutagens in Normal and p53-mutated Human Lymphoblastoid Cells" <i>Mut. Res.</i> , 1997 , 374, 89-98.	
mmf		Jiricny, J., et al., "Mismatch repair defects in cancer" <i>Curr. Opin. Genet. Dev.</i> , 2000 , 10, 157-161.	
mmf		Karran, P., et al., "Genomic instability and tolerance to alkylating agents" <i>Cancer Surveys</i> , 1996 , 28, 69-71.	
mmf		Leach, F.S., et al., "Mutations of a mutS homolog in hereditary nonpolyposis colorectal cancer" <i>Cell</i> , 1993 , 75, 1215-1225.	
mmf		Li, G.-M. and P. Modrich. "Restoration of mismatch repair to nuclear extracts of H6 colorectal tumor cells by a heterodimer of human MutL homologs" <i>Proc. Natl. Acad. Sci. USA</i> 1995 92:1950-1954.	
mmf		Liu, W. et al., "Microsatellite instability as a predictor of a mutation in a DNA mismatch repair gene in familial colorectal cancer" <i>Genes, Chromosomes & Cancer</i> , 2000 , 27, 17-25.	

Examiner Signature	<i>mmf</i>	Date Considered	July 12, 2002
--------------------	------------	-----------------	---------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Please type a plus sign (+) inside this box →



PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

3

of

5

Complete if Known

Application Number	09/780,675
Filing Date	February 12, 2001
First Named Inventor	NICOLAIDES et al
Group Art Unit	1641 1636
Examiner Name	Unassigned
Attorney Docket Number	01107.00098

RECEIVED
AUG 20 2001
TECH CENTER 1600/2900

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
duplicate		Liu, T., et al., "Microsatellite instability as a predictor of a mutation in a DNA mismatch repair gene in familial colorectal cancer" <i>Genes, Chromosomes & Cancer</i> , 2000, 27, 17-25.	
nmf		Liu et al., "Analysis of Mismatch Repair Genes in Hereditary Non-polyposis Colorectal Cancer Patients" <i>Nature Medicine</i> , February 1996, 2(2), 169-174.	
nmf		Ma et al., "Dominant Negative Expression of hPMS2 Creates Isogenic Mismatch Repair Deficient Human Colon Cancer Cell Lines" <i>Proc. Am. Assoc. Cancer Res.</i> , March 1998, 39, p. 460 (Abstract #3130).	
nmf		McCallum, C.M., "Targeted screening for induced mutations" <i>Nature Biotechnology</i> , 2000, 18, 455-457.	
nmf		Modrich, P., "Mismatch repair, genetic stability, and cancer" <i>Science</i> , 1994, 266, 1959-1960.	
nmf		Nicolaides, N.C., et al., "The Jun family members, c-Jun and JunD, transactivate the human c-myc, promoter via an Ap1-like element" <i>J. Biological Chemistry</i> , 1992, 267(27), 19655-19672.	
nmf		Nicolaides, N.C., et al., "Genomic organization of the human PMS2 gene family" <i>Genomics</i> , 1995, 30, 195-206.	
nmf		Nicolaides, N.C. et al. "Molecular cloning of the N- terminus of GTBP." <i>Genomics</i> 1996, 31:395-397.	
nmf		Nicolaides, N.C., et al., "Positive autoregulation of c-myc, expression via Myb binding sites in the 5' flanking region of the human c-myc gene" <i>Molecular and Cellular Biology</i> , 1991, 11(12), 6166-6176.	
nmf		Nicolaides, N.C., "A naturally occurring hPMS2 mutation can confer a dominant negative mutator phenotype" <i>Mol. Cell. Biol.</i> , 1998, 18(3), 1635-1641.	
nmf		Nicolaides, N.C., et al., "Analysis of the 5' region of PMS2 reveals heterogeneous transcripts and a novel overlapping gene" <i>Genomics</i> , 1995, 29, 329-334.	

Examiner
Signature

nmf

Date
Considered

July 12, 2002

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Please type a plus sign (+) inside this box → +



PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no person is required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Complete if Known	
		Application Number	09/780,675
		Filing Date	February 12, 2001
		First Named Inventor	NICOLAIDES et al.
		Group Art Unit	164T 1630
		Examiner Name	Unassigned
		Attorney Docket Number	01107.00098
Sheet	4	of	5

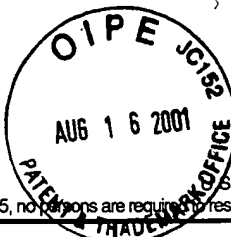
OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
TMJ		Nicolaides, N.C., et al., "Mutations of two PMS homologues in hereditary nonpolyposis colon cancer" <i>Nature</i> , 1994 , 371, 75-80.	
TMJ		Palombo, F., et al., "Mismatch repair and cancer" <i>Nature</i> , 1994 , 367, 417.	
TMJ		Pang, Q., T.A. Prolla and R.M. Liskay, "Functional domains of the <i>Saccharomyces cerevisiae</i> Mlh1p and Pms1p DNA mismatch repair proteins and their relevance to human hereditary nonpolyposis colorectal cancer-associated mutations" <i>Mol. Cell. Biol.</i> 1997 17(8):4465-4473.	
TMJ		Papadopoulos, N., et al., "Mutation of a <i>mutL</i> homolog in hereditary colon cancer" <i>Science</i> , 1994 , 263, 1625-1629.	
TMJ		Papadopoulos, N., et al., "Mutations of <i>GTBP</i> in genetically unstable cells" <i>Science</i> , 1995 , 268, 1915-1917.	
TMJ		Parsons, R. et al. "Mismatch repair deficiency in phenotypically normal human cells." <i>Science</i> 1995 268:738-740.	
TMJ		Parsons, R., et al., "Hypermutable and mismatch repair deficiency in RER+ tumor cells" <i>Cell</i> , 1993 , 75, 1227-1236.	
TMJ		Peinado, M.A., et al., "Isolation and characterization of allelic losses and gains in colorectal tumors by arbitrarily primed polymerase chain reaction" <i>Proc. Natl. Acad. Sci. USA</i> , 1992 , 89, 10065-10069.	
TMJ		Perucho, M., et al., "Cancer of the microsatellite mutator phenotype" <i>Biol. Chem.</i> , 1996 , 377, 675-684.	
TMJ		Prolla, T.A., et al., "MLH1, PMS1, and MSH2 interactions during the initiation of DNA mismatch repair in yeast" <i>Science</i> , 1994 , 265, 1091-1093.	
TMJ		Quian, Y. et al., "Molecular events after antisense inhibition of hMSH2 in a HeLa cell line" <i>Mutation Research</i> , October 12, 1998 , Vol. 418, pp. 61-71.	

Examiner Signature		Date Considered	July 12, 2002
-----------------------	--	--------------------	---------------

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Please type a plus sign (+) inside this box →

+



PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

5

of

5

Complete if Known

Application Number	09/780,675
Filing Date	February 12, 2001
First Named Inventor	NICOLAIDES et al.
Group Art Unit	1641 1036
Examiner Name	Unassigned
Attorney Docket Number	01107.00098

RECEIVED
AUG 20 2001
TECH CENTER
1600/2900

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
AMT		Spampinato, C., et al., "The MutL ATPase is required for mismatch repair" <i>J. Biological Chemistry</i> , 2000 , 275(13), 9863-9869.	
AMT		Strand, M., et al., "Destabilization of tracts of simple repetitive DNA in yeast by mutations affecting DNA mismatch repair" <i>Nature</i> , 1993 , 365, 274-276.	
AMT		Su, S., et al., "Mispair specificity of methyl-directed DNA mismatch correction <i>in vitro</i> " <i>J. Biological Chemistry</i> , 1988 , 263(14), 6829-6835.	
AMT		Vora, K.A. et al., "Severe Attenuation of the B Cell Immune Response in Msh2-deficient Mice" <i>Journal of Experimental Medicine</i> , February 1999 , 189(3), 471-481.	
AMT		Wheeler, J.M.D., et al., "The role of hypermethylation of the <i>hMLH1</i> promoter region in HNPCC versus MSI+sporadic colorectal cancers" <i>J. Med. Genet.</i> , 2000 , 588-592.	
AMT		Winter, D.B. et al., "Altered spectra of hypermutation in antibodies from mice deficient for the DNA mismatch repair protein PMS2" <i>Proc. Natl. Acad. Sci., USA</i> , June 1998 , 95, 6953-6958.	

Examiner
Signature

[Handwritten Signature]

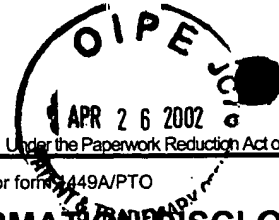
Date
Considered

July 12, 2002

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)			Complete if Known	
			Application Number	09/780,675
			Filing Date	February 12, 2001
			First Named Inventor	Nicholas C. Nicolaides et al.
			Group Art Unit	1641
			Examiner Name	TBA
Sheet 1 of 1	Attorney Docket Number	001107.00098		

U.S. PATENT DOCUMENTS					
Examiner Initials *	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code ² (if known)			
		US-			
		US-			

FOREIGN PATENT DOCUMENTS							
Examiner Initials*	Cite No. ¹	Foreign Patent Document		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ - Number ⁴ - Kind Code ⁵ (if known)					

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
mmf		Fishel, R. et al., "The Human Mutator Gene Homolog MSH2 and its Association with Hereditary Nonpolyposis Colon Cancer", <u>Cell</u> , Vol. 75, pp. 1027-1038 (1993)	
mmf		Prudhomme, M. et al., "Mismatch Repair Genes of <i>Streptococcus pneumoniae</i> : HexA Confers a Mutator Phenotype in <i>Escherichia coli</i> by Negative Complementation", <u>Journal of Bacteriology</u> , Vol. 173, No. 22, pp. 7196-7203, (1991)	
mmf		Aronsham, Al. et al., "Dominant Negative Mutator Mutations in the mutL Gene of <i>Escherichia coli</i> ", <u>Nucleic Acids Research</u> , Vol. 24, No. 13, pp. 2498-2504 (1996)	
mmf		Bornscheuer, U. et al., "Directed Evaluation of an Esterase for the Stereoselective Resolution of a Key Intermediate in the Synthesis of Epothilones", <u>Biotechnology and Bioengineering</u> , Vol. 58, No. 5, pp. 554-559 (1998)	
mmf		Loh, T. et al., "Mutational Analysis of the Muth Protein from <i>Escherichia coli</i> ", <u>The Journal of Biological Chemistry</u> , Vol. 275, No. 15, pp. 12113-12119 (2001)	
mmf		Horst, J.P. et al., " <i>Escherichia coli</i> Mutator Genes", <u>Trends in Microbiology</u> , Vol. 7, No. 1, pp. 29-36 (1999)	
mmf		Fijalkowska, I. et al., "Mutants in the Exo I Motif of <i>Escherichia coli</i> /DNAQ: Defective Proofreading and Inviability due to Error Catastrophe", <u>Proc. Natl. Acad. Sci.</u> , Vol. 93, pp. 2856-2861 (1996)	

RECEIVED

APR 29 2002

Examiner Signature	<i>mmf</i>	Date Considered	July 11, 2002
--------------------	------------	-----------------	---------------

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04.

³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.